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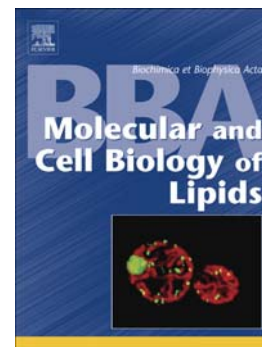
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The Physics of Lipid Droplet Nucleation, Growth and Budding

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Abstract:

Lipid droplets (LDs) are intracellular oil-in-water emulsion droplets, covered by a phospholipid monolayer and mainly present in the cytosol. Despite their important role in cellular metabolism and growing number of newly identified functions, LD formation mechanism from the endoplasmic reticulum remains poorly understood. To form a LD, the oil molecules synthesized in the ER accumulate between the monolayer leaflets and induce deformation of the membrane. This formation process works through three steps: nucleation, growth and budding, exactly as in phase separation and dewetting phenomena. These steps involve sequential biophysical membrane remodeling mechanisms for which we present basic tools of statistical physics, membrane biophysics, and soft matter science underlying them. We aim to highlight relevant factors that could control LD formation size, site and number through this physics description. An emphasis will be given to a currently underestimated contribution of the molecular interactions between lipids to favor an energetically costless mechanism of LD formation.

Highlights

- Lipid droplet biogenesis occurs in three steps: nucleation, growth and budding
- Phase separation and dewetting phenomena are determinant for lipid droplet formation
- Interactions between lipids allow for spontaneous lipid droplet nucleation and budding

I Introduction

Lipid droplets (LDs) are dynamic organelles found in almost all organisms. They have an oil core, consisting of triglycerides (TG) and sterol esters (SE), surrounded by a phospholipid (PL) monolayer containing proteins[1-3]. From the physical chemistry standpoint, LDs represent an inverted emulsion, meaning a solution of oil-in-water droplets[4]. Despite an important role in energy metabolism and cellular homeostasis[1], and an expanding list of newly identified functions[5], the mechanism of LD formation remains largely unknown[3, 6-10]. Under nutrient rich conditions, excess metabolites are transformed mainly into TG and SE molecules, depending on

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